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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
NGUYEN, QUANG	
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1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/905,114	Applicant(s) ZHANG ET AL.	
	Examiner Quang Nguyen, Ph.D.	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) *8 and 17-56* is/are withdrawn from consideration.

5)☒ Claim(s) *1-6* is/are allowed.

6)☒ Claim(s) *7,9 and 11-16* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6, 7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-56 are pending in the present application.

Applicants' election with traverse the invention of Group I (claims 1-7 and 9-16) in Paper No. 9 is acknowledged. Applicants traverse on the grounds that the Office has not shown that a burden exists in searching all the claims of the present application, and that the International Searching Authority did not take the position that unity of invention was lacking in the International application, and examined all claims together. Applicants' arguments are respectfully found to be unpersuasive because the claims are drawn to distinct or independent subject matters or inventions as set forth in the Restriction requirement in Paper No. 8, and that the searches for all the inventions within a single application would be unduly burden for the Examiner. Examiner also would like to note that the criteria for determining the lack of unity of invention in an international application are not the same as those required for restriction in a U.S. application, and that Applicants have not provided any arguments on why the inventions are not properly distinct or independent. It is noted that claims 17, 24 and 55 link a plurality of patentably distinct groups of mammalian and avian sperm cells, and distinct groups of transgenic non-human mammal and transgenic avian that lack the unity of invention because they do not share a substantial common core structure or element among themselves, and therefore group restrictions and not species restrictions are set forth in the previous Office Action.

Accordingly, claims 8 and 17-56 are withdrawn from further consideration because they are drawn to non-elected inventions.

Claims 1-7 and 9-16 are examined on the merits herein.

Sequence Compliance

It is noted that an adaptor primer having a nucleotide sequence longer than 9 nucleotides has not been assigned a SEQ ID NO. (see page 9, lines 1-2), nor does the exemplified amino acid sequence in Fig. 1 having more than 3 amino acid residues. Appropriate correction is required to comply with the sequence rules.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 9 and 11-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

Applicant's invention is drawn to an isolated polynucleotide which hybridizes under stringent conditions to an isolated polynucleotide sequence comprising SEQ ID NO:1 or SEQ ID NO:3 and encodes a fertility associated antigen (FAA). Applicant's invention is also drawn to a method of producing a fertility associated antigen comprising an isolated polynucleotide encoding fertility associated antigen into a host cell, culturing said host cell under conditions suitable for expression of fertility associated antigen, and isolating the fertility associated antigen produced. The scope of the present invention encompasses a method of producing a fertility associated antigen using any isolated polynucleotide encoding fertility associated antigen, not necessarily limited to one that has greater than 70% identity to SEQ ID NO:1, and any isolated polynucleotide encoding a fertility associated antigen as long as it hybridizes to SEQ ID NO:1 or SEQ ID NO:3 under stringent conditions. Apart from disclosing the partial bovine cDNA sequence comprising SEQ ID NO:1 or SEQ ID NO:3, the instant specification fails to teach which essential core structures or elements that any of the claimed isolated polynucleotide hybridized to SEQ ID NO:1 or SEQ ID NO:3 under stringent conditions would need to possess in order to code for a polypeptide having one or more bioactivities associated with natural fertility associated antigen (e.g., cryo-protective property and/or enhancing fertility of a sperm), so that it can be utilized in a method for producing a fertility associated antigen. The claims also encompass any isolated polynucleotide molecule encoding a fertility associated antigen from any animal

species or existing in nature that has yet been isolated and characterized. Kennell (Progr. Nucl. Acid Res. Mol. Biol. 11:259-301, 1971) states that "it would appear that, depending on G + C content, the minimum size for a stable complex is from 10 to 20 nucleotides. The thermal stability rises sharply for longer lengths so that, depending on the G + C content, the stability of a complementary duplex of 25-50 nucleotides approaches that of any much longer complex" (page 261, first paragraph). Therefore, would any polynucleotide sequence that is capable of forming a complementary duplex of 25-50 identical nucleotides to SEQ ID NO:1 or SEQ ID NO:3 encode for a fertility associated antigen? Additionally, it is well recognized in the art that any modification (even a "conservative" substitution) to a critical structural region of a polypeptide is likely to significantly alter its functional properties. The present disclosure offers no written description as to which regions of the encoded FAA molecule would be tolerant of alteration and which would not, which "particular" encoded amino acid changes (substitution, deletion or insertion) at which positions and in which combinations, such that the encoded variant FAA proteins still possess one or more of the bioactivities of natural FAA. Moreover, the instant specification fails to teach a representative number of species for a broad genus of a polynucleotide encoding a fertility associated antigen. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants' filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics

such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structures of any isolated polynucleotide encoding a fertility associated antigen, other than a polynucleotide sequence comprising SEQ ID NO:1 or SEQ ID NO:3 and a method for producing a FAA using the same. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 7, 9 and 11-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide sequence comprising SEQ ID NO:1 or SEQ ID NO:3 which encodes a fertility associated antigen, and a method of producing a fertility associated antigen in a cultured host cell using the same; does not reasonably provide enablement for other embodiments of the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in the determination of an enabling disclosure have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex parte Forman*, (230 USPQ 546 (Bd Pat. Appl & Unt, 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)).

Claim 7 is drawn to an isolated polynucleotide, which hybridizes under stringent conditions to an isolated polynucleotide sequence comprising SEQ ID NO:1 or SEQ ID NO:3 and encodes a fertility associated antigen.

Claims 9 and 11-16 are drawn to a method of producing a fertility associated antigen comprising introducing an isolated polynucleotide encoding fertility associated antigen into a host cell, culturing said host cell under conditions suitable for expression of fertility associated antigen, and isolating the fertility associated antigen produced; the same method with various limitations in the dependent claims.

With respect to the elected invention, the specification discloses by exemplification the cloning a partial cDNA sequence (SEQ ID NO:1) encoding the 22 kDa bovine fertility associated antigen (FAA) having amino acids 73 to 269 of the natural intact bovine FAA. Applicants further demonstrate that the recombinant 22 kDa FAA reduces cryo-damage to the bull sperm and increases fertility of the sperm when used as a semen additive.

The above evidence has been noted and considered. However, the evidence is not reasonably extrapolated to the instant broadly claimed invention for the following reasons.

As defined by the present application, polynucleotides which encode the FAA mean the sequences exemplified in this application as well as those sequences which have substantial identity to SEQ ID NO:1 and which encode a molecule having one or more of the bioactivities of natural FAA (see specification, page 4, lines 13-16). Therefore, the instant claims encompass any isolated polynucleotide variant of SEQ ID NO:1, preferably at least 70%, 80%, 90 or 95% identity to SEQ ID NO: 1 or well below 70% identity to SEQ ID NO:1, and that the polynucleotide variant encodes a molecule having one or more of the bioactivities of natural FAA, and methods for producing a fertility associated antigen in a cultured host cell using the same. The instant specification is not enabled for such a broadly claimed invention for the same reasons already discussed in the lack of Written Description above. Briefly, in order to make any sequence variant with the reasonable assurance that it would have the desirable properties of the invention, the artisan would need to know which region(s) of the molecule are responsible for the interactions underlying its biological functions. As is well recognized in the art, any modification (even a "conservative" substitution) to a critical structural region of a protein is likely to significantly alter its functional properties. The present disclosure offers no guidance as to which regions of the encoded FAA molecule would be tolerant of alteration and which would not, which "particular" amino acid changes (substitution, deletion or insertion) at which positions and in which

combinations, such that the encoded variant FAA proteins having one or more of the bioactivities of natural FAA could still be retained. There is a high degree of unpredictability associated with the make and use of the claimed embodiment. In discussing peptide hormones, Rudinger has stated that "The significance of particular amino acids and sequences for different aspects of biological activity can not be predicted a priori but must be determined from case to case by painstaking experimental study (Page 6, first sentence of Conclusions *In* J.A. Parsons, ed. "Peptide hormones", University Park Press, 1976). This unpredictability is further underscored by the fact that the relationship between the sequence of a peptide and its tertiary structure (or its activity) is not well understood and is not predictable (Ngo et al., *In* K. Merz et al., ed. "The protein folding problem and tertiary structure prediction", Birkhauser, 1994, 491-495). Moreover, the physiological art is recognized as unpredictable (MPEP 2164.03). As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> That scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the are; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

Additionally, the Board and Court have held in several instances that the disclosure of a single amino acid sequence is not sufficient to enable claims directed to any functionally equivalent variants of that sequence. See, for example, *Amgen v. Chugai*, 18 USPQ2d 1016 (Fed. Cir. 1991); *Ex parte Maizel*, 27 USPQ2d (BPAI 1993).

Therefore, due to the lack of guidance and examples provided by the instant specification, it would have required undue experimentation for one skilled in the art to make and use the claimed invention in its full scope.

Accordingly, due to the lack of sufficient guidance provided by the specification, regarding to the issues discussed above, the unpredictability of the physiological art, particularly the unpredictable relationship between the sequence of a peptide and its tertiary structure or its activity, and the breadth of the instant claims, it would have required undue experimentation for one skilled in the art to make and use the instant broadly claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 7, it is unclear what is encompassed by the phrase "under stringent conditions". This is because certain hybridization conditions would be considered to be stringent by an ordinary skilled artisan but not by another ordinary skilled artisan. Therefore the metes and bounds of the claim are not clearly determined.

Conclusions

At the effective filing date of the present application, the prior art does not teach or fairly suggest an isolated polynucleotide sequence comprising SEQ ID NO:1 or SEQ ID NO:3, a vector and a host comprising the same.

Claims 1-6 are allowable. Claim 10 is objected because it is dependent on the rejected claim 9.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, Gerald Leffers, Jr., Ph.D., may be reached at (703) 305-6232, or SPE, Irem Yucel, Ph.D., at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to LIE, Tiffany Tabb, whose telephone number is (703) 605-1238.

Quang Nguyen, Ph.D.

Gerald D. Leffers
PATENT EXAMINER